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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,616	05/16/2001	Hans-Ulrich Bernard	REF/BERNARD	6676

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 02/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/763,616	Applicant(s) BERNARD ET AL.	
	Examiner Brian S Kwon	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,14,17-20,22-35 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14,17-20,22-35 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *16* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Summary of Action

I. The objection of claim 22 will not be maintained in light of the amendment.

II. The rejection of claim 23 under 35 USC 112, second paragraph, will not be maintained in light of the amendment.

III. The rejection of claim 40 under 35 USC 102(b) as being anticipated by Tran et al. will not be maintained in light of the amendment.

IV. The rejection of claim 13, 14, 17-20, 23-35 and 40 under 35 USC 112, first paragraph, will be maintained for the reason of the record.

V. The rejection of claims 13-14, 20, 31, 32, 33 and 40 under 35 USC 102(b) as being anticipated by Rotstein et al. will be maintained for the reason of the record.

Information Disclosure Statement

1. Acknowledgment is made of applicant's filing of non-patent publications in PTO form-1449 dated September 11, 2003. Applicants state that those are not cited as references but in support of the level of one of ordinary skill in the art. Accordingly, it has been placed in the application file, but the information referred to therein has not been considered as to the merits. In any case, applicants desire for the examiner to consider those references, applicants is advised to file the information disclosure statement in compliance with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609.

Status of Application

2. By Amendment filed September 11, 2003, Claims 1-12 and 36-39 have been cancelled and Claims 13, 16, 18, 20-23 and 32 have been amended. Claims 13-35 and 40 are currently pending for prosecution on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 13-14, 17-20, 23-35 and 40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

This rejection is analogous to the original rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 13-14, 20, 22-23, 31, 32, 33 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Rotstein et al. (Carcinogenesis, 1988, 9(9), 1547-51).

This rejection is analogous to the original rejection.

Response to Arguments

Applicant's arguments filed September 11, 2003 have been fully considered but they are not persuasive.

5. Applicant's argument takes position that the potential suitability of a compound can be determined by directly or indirectly measuring the amount of a metal cation released when the compound is contacted with a protein molecule containing a chelated metal cation domain by means of performing TSQ, BIOCORE and WSTI assays described in the specification. Applicant alleges that the determination of whether the compounds fall within the scope of claim 40 or not would be readily apparent to those skilled in the art without undue amount of experimentation. The examiner disagrees. Unlike applicant's allegation, the potentially suitable compounds interested in this invention and tested for their activity in "facilitating the disruption of chelated metal cation domain" are only limited to the compounds represented by the formula (I) or (II). Applicants fail to provide sufficient information or guidance allowing the skilled artisan to make and use the claimed full scope of "a compound capable of facilitating the disruption of a chealted

metal cation domain of a protein encoded for by an MPV gene" other than the disclosed compounds represented by the formula (I) or (II). Therefore, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine all potential compounds "capable of facilitating the disruption of a chelated metal cation domain" that would be enabled in this specification.

6. With respect to applicant's argument regarding "one of ordinary skill in the art would recognize that although compounds which exhibit activity in all 3 of the described assays might be preferred (see page 23, lines 21-26) other compounds of formula (I) and (II) administered as a pharmaceutically acceptable derivative may be effective in inhibiting the growth of MPV cell lines", the examiner agrees with applicant that such could be determined by routine experimentation.

7. Applicant's argument takes position that one of ordinary skill in the art would recognize that a compound which disrupts the E6 and/or E7 zinc fingers would reasonably be expected to treat a disease or condition caused by an HPV since (i) the oncogenes E6 and E7 of HPV types are homologous and have similar functions; and (ii) the E6 and E7 proteins are essential for the formation and persistence of HPV-associated lesions and the zinc fingers of HPV E6 and/or E7 are required for their cellular function. The examiner agrees that the HPV genome contain 8 genes comprised of 6 early genes (E1, E2, E4, E5, E6 and E7) and 2 late genes (L1 and L2) and the oncogenes E6 and E7 of HPVs are homologous and have similar functions as E6 and E7 of HPV 16 and HPV 18. However, the examiner disagrees that the disruption of E6 and/or E7 zinc fingers by the compounds would provide reasonable expectation to one of ordinary skill in the art to recognize that the claimed compounds can treat all the claimed condition or disease caused

by all HPVs, more broadly the claimed genus of mammalian papilloma viruses (MPV) as the claimed invention. There is no sufficient information provided in the specification that oncogenes E6 and E7 of HPVs are definite contributing factor for the entire scope of the claimed disease conditions by MPV. Furthermore, in light of the state of art at the time of the invention was made that there is no absolute correlation between the activity of HPV E6 and/or E7 proteins and the development of all of the claimed conditions caused by mammalian papilloma viruses (MPV). The specification provides insufficient written description to support the genus encompassed by the claim. Furthermore, the specification does not clearly provide an adequate representation regarding how to prevent or cure the disease conditions. The state of the art recognizes the treatment of symptoms of the specific disorders such as cervical cancer, cervical intraepithelial neoplasia or squamous intraepithelial lesions or genital warts but not their cure. Thus, the skilled artisan cannot envision the claimed method of preventing said disease condition in animal without significant guidance from the specification or prior art to prevent or cure the diseases or conditions as required in the instant claims. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for preventing it.

8. Applicant's argument takes position that the referenced antisense ODNs (taught in Tran et al.) does not fall on the scope of the compound which facilitates the disruption of a chelated metal cation domain of a protein encoded for by an MPV gene since the antisense ODNs involve the use of short complementary oligonucleotides to interfere with the function of mRNAs. This argument is found persuasive. Therefore, the examiner withdraws this rejection.

9. Applicant's argument takes position that Rotstein's teaching of using disulfiram (a compound of formula II) in inhibiting tumor progression by acting as antioxidants differs from those of the compounds described in the instant invention that are drawn to "facilitating the disruption of chelated metal cation domain of a protein encoded for by an MPV gene". The examiner agrees with applicant that the mechanism of action for the instant invention and that described by Rotstein are different. However, the reference directing the administration of same composition inherently possessing a therapeutic effect for the same ultimate purpose as disclosed by Applicant anticipates Applicant's claims even absent explicit recitations of the mechanism of action. The fact that the applicant may have discovered a new pharmacological mechanism for the claimed compound is not considered patentably distinctive over the prior art which are directed to the same therapeutic application.

Conclusion

10. Applicant's amendment necessitated a new ground of rejection in this Office action. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703) 308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600